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(71) Applicant *(for all designated States except US)*: **PYROSEQUENCING AB** [SE/SE]; Vallongatan 1, S-752 28 Uppsala (SE).

(71) Applicant *(for MG only)*: **SAMUELS, Adrian, James** [GB/GB]; Frank B. Dehn & Co., 179 Queen Victoria Street, London EC4V 4EL (GB).

(72) **Inventors; and**
(75) **Inventors/Applicants** *(for US only)*: **ANDERSSON, Helen** [SE/SE]; Fleminggatan 25, S-112 26 Stockholm (SE). **STEMME, Göran** [SE/SE]; Ruddammsvägen 31B, S-114 21 Stockholm (SE). **VAN DER WIJNGAART, Wouter** [BE/SE]; Fleminggatan 25, S-11226 Stockholm (SE).

(74) Agent: **FRANK B. DEHN & CO.**; 179 Queen Victoria Street, London EC4V 4EL (GB).

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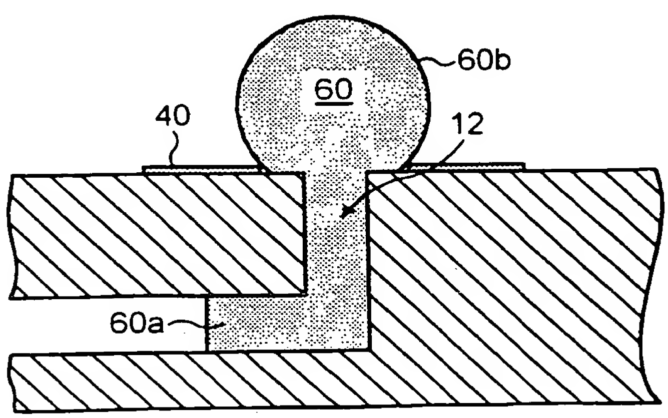
(54) **Title:** INLET FOR MICROFLUIDIC DEVICES



(57) **Abstract:** A microfluidic device comprises a liquid inlet having an inlet mouth (12) and liquid confinement means (40, 50) provided around the inlet mouth (12) to confine liquid (60) placed at the mouth to a predetermined area (55) around the mouth. The liquid confinement means (40, 50, 52) could be a hydrophobic material (50) or geometrical structure such as a channel (50) or recess (52) around the inlet, or a combination of both. Also disclosed is liquid confinement means around an array of liquid inlets which may or may not have their own liquid confinement means.

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INLET FOR MICROFLUIDIC DEVICES

This invention relates to microfluidic devices, and methods of facilitating transfer of liquids onto and the storage of liquids on such devices.

Conventionally, reactions involving a liquid reagent, such as large numbers of assays or the like, are carried out using microtiter plates. A microtiter plate is a plastics plate with a number of wells, closed at the bottom and capable of holding a certain volume of liquid. Liquid reagents are added to the wells manually with pipettes, or by a robot. Microtiter plates are inexpensive and generally convenient, although do suffer from some drawbacks. For example, since the wells are each essentially a closed system, the by-products of any reactions which take place will accumulate in the wells. Another drawback is that the wells of a microtiter plate are relatively large in volume and thus may not be very suitable for reactions which utilise small volumes of liquid.

It is also known to use micro-machined silicon chips for chemical analysis. These are normally planar with inlet and outlet holes formed to provide access to the interior of the chip. In order to interface with such chips, it is common to glue interconnecting tubes onto the inlets and outlets. However, this itself causes several problems.

Firstly, it is difficult to align the interconnecting tubes to the inlet/outlet holes. Secondly, there is the danger that the inlet or outlet hole could accidentally be filled with glue. Furthermore, interconnecting tubes usually introduce relatively large dead volumes into the system which is undesirable in the context of low volume assays. Finally, the glueing process must be carried out

manually and is therefore relatively labour intensive.

Furthermore, the applicant has realised that such micro-machined systems are essentially two dimensional which means that only very small volumes of liquid may be stored on the chips without taking up a large surface area. It has also been appreciated that there exists a considerable risk of overflow and therefore cross-contamination in micro-array chip systems.

The present invention aims to provide an improved arrangement and when viewed from a first aspect provides a microfluidic device comprising a liquid inlet having an inlet mouth and liquid confinement means provided around said inlet mouth to confine liquid placed at said mouth to a predetermined area around the mouth. Thus it will be seen by those skilled in the art that in accordance with the present invention, liquid may be more easily introduced to a fluid inlet of a microfluidic device with a reduced risk of overflow and cross-contamination since this is prevented by the fluid confinement means.

Furthermore, since the contact area between a drop of liquid applied to the mouth of the fluid inlet is confined to be within a predetermined area inside the liquid confinement means, for a given surface area a larger volume drop than hitherto may be stored on the device at the inlet mouth by virtue of the surface tension of the drop. It will be appreciated that this is advantageous since more liquid than may be accommodated in the fluid inlet itself may be stored on the device at the inlet mouth and drawn into the fluid inlet as required, e.g. by applying a suitable suction force. In other words each inlet may be provided with its own reservoir.

In accordance with a first set of preferred embodiments, the liquid confinement means may comprise a region of hydrophobic material. It should be understood that the term "hydrophobic material" is intended to

denote a material with greater hydrophobicity than the surrounding surface of the device and does not connote any particular absolute level of hydrophobicity.

Preferably the hydrophobic material comprises lithographically defined hydrophobic patches on the substrate of the device. For example, the device may be of silicon with channels to receive the hydrophobic patches being formed by Deep Reactive Ion Etching (DRIE). In preferred embodiments, the hydrophobic material comprises silicone or octafluorocyclobutane (C_4F_8).

In an alternative set of embodiments, the liquid confinement means may comprise a suitable geometric structure, preferably defined by the substrate of the microfluidic device. In one preferred example, the liquid confinement means comprises a change in surface height of the device. For example, the inlet mouth and the area around it to which the liquid is to be confined, may be located in a recess on the device with the liquid confinement means being defined by the side walls of the recess. Alternatively, the edge of the confinement area may be defined by a channel around the inlet mouth. Of course, it will be appreciated that the liquid confinement means may comprise any combination of the above.

The principles of the present invention may also bring benefit if they are applied to more than one inlet. For example, it may be desirable in some circumstances always to apply liquid simultaneously to two or more liquid inlets. In this case, it need be necessary only to confine the liquid to within an area surrounding two or more inlet mouths since cross-contamination between these fluid inlets is not an issue.

Thus, when viewed from a second aspect, the invention provides a microfluidic device comprising an array of liquid inlets and liquid confinement means

provided around said array of inlets to confine liquid placed on said array to a predetermined area around the array.

The preferred forms of the liquid confinement means set out above in relation to the first aspect of the invention apply equally to the liquid confinement means of the present aspect of the invention.

The individual liquid inlets within the array may simply be formed as in known arrangements. Preferably, however, at least one or more and preferably all of the liquid inlets further comprise liquid confinement means around them. This gives a highly flexible arrangement in which liquid may be applied individually or to a sub-group of the fluid inlets in the array by applying an appropriate volume; or alternatively a liquid may be applied simultaneously to all of the inlets within the array simply by applying a higher volume of liquid. In particular, this may be achieved by applying a volume of liquid greater than the sum of the volumes which may be stored by the liquid confinement means at the individual fluid inlet mouths.

The fluids confinement means surrounding the individual fluid inlet mouths may be of the same form as that around the array, of a different form but the same as one another or may, as convenient, be of separate forms.

In accordance with all of the above-mentioned aspects of the invention, the microfluidic device preferably comprises a micro-machined substrate, preferably of or comprising silicon. In the most preferred embodiment, the substrate is formed using Deep Reactive Ion Etching (DRIE).

Certain preferred embodiments of the present invention will now be described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 shows schematically a fluid inlet of a microfluidic device embodying the present invention;

Figure 2 shows the fluid inlet of Figure 1 after the application of a drop of liquid;

Figure 3 shows schematically a fluid inlet of a second embodiment of the invention;

Figure 4 shows the fluid inlet of Figure 3 after the application of a draft liquid;

Figure 5 shows schematically two fluid inlets of a third embodiment of the invention;

Figure 6 shows a fourth embodiment of the invention;

Figure 7 shows a further embodiment employing two types of liquid confinement means;

Figure 8 shows the embodiment of Figure 7 after the application of a small drop of liquid;

Figure 9 shows the embodiment of Figure 7 after the application of a large drop of liquid; and

Figures 10 to 12 show further possible embodiment of the invention.

Turning firstly to Figure 1, there may be seen a close- up, cross-sectional view of a microfluidic device in accordance with a first embodiment of the invention.

The device comprises a substrate 10 in which a fluid inlet duct 25 is formed. by. The fluid duct 25 conveys liquid to a reaction chamber in the device (not shown). Around the mouth 12 of the fluid inlet, there is provided an annular ring of hydrophobic material 40 which comprises octafluorocyclobutane (C_4F_8). The hydrophobic material 40 has a greater hydrophobicity than the surface 15 of the device which surrounds it. The hydrophobic material 40 defines a confinement area 55 within it.

The device shown in Fig 1 is fabricated using Deep Reactive Ion Etching (DRIE) of 525 micrometre thick p-doped silicon wafers in a standard ion-coupled plasma etcher (Surface Technology Systems, UK) using 1.5 micrometre thick photoresist as the etch mask.

Figure 2 shows the fluid inlet after a drop of

liquid 60 has been applied to it. As will be seen, the hydrophobic patch 40 confines the area of contact between the liquid 60 and the surface 15 of the substrate to within the confinement area 55. This allows some liquid 60a to enter the inlet duct 25 whilst surface tension retains the remainder of the liquid 60 in a bulb 60b outside the inlet duct 25. Thus, as liquid is drawn into the inlet duct 25 during use and expelled through an outlet duct (not shown) the bulb 60b will supply further liquid. It will therefore be seen that a significantly increased volume of liquid may be stored on the device but taking up relatively little surface area. In a particular example it was found that

A second embodiment of the invention is shown in Figures 3 and 4. In this arrangement, the confinement area 55 is defined by an annular channel 50 around the mouth 12 of the inlet duct. The channel 50 has precisely the same effect as the hydrophobic patch of the previously described embodiment in that it prevents the liquid 60 from spreading outside the confinement area 55 thereby preventing cross-contamination and facilitating storage of liquid in a bulb 60b above the inlet mouth 12, as is clear from Figure 4.

Figure 5 shows a further embodiment which is similar to that shown in Figures 1 and 2 except that, in this embodiment, the confinement area 30 includes an array of fluid inlet mouths 12, two of which may be seen in Figure 5. In this embodiment, a larger volume of liquid is placed onto the confinement area 30 and may thus enter all of the fluid inlet mouths 12 within the confinement area simultaneously. It will also be appreciated that an even larger volume of liquid may be stored above the upper surface 15 of the device before it is drawn in to the fluid inlet ducts 25 to be used.

The embodiment in Figure 6 depicts a further possible arrangement for a confinement area 30 which includes an array of fluid inlets 25. In this

embodiment, the mouths 12 of the fluid inlets are located within a recess in the substrate 10 of the device, the walls 50 of which define the edges of the confinement area 30. As with the previous embodiment, liquid placed in the confinement area may be stored before it is required and drawn in to the individual fluid inlets 25 simultaneously through capillary action or, alternatively, could be drawn selectively only into some of the fluid inlets 25 by applying a suction force on those particular inlets.

Figure 7 shows a further embodiment of the invention which combines the features of the embodiment of Figure 1 with those of the embodiment of Figures 3 and 4. Thus, two fluid inlet mouths 12 are individually surrounded by channels 50 defining confinement areas 55. Furthermore however, a region of hydrophobic material in the form of silicone tape 42 is provided around the array of fluid inlets 25. This defines a larger confinement area which encompasses the array of fluid inlet mouths 12.

In accordance with this embodiment, a relatively small volume of liquid may be applied to the individual fluid inlet mouths 12 as shown by the dashed outlines 62. In this configuration, different liquids may be applied to each of the fluid inlet mouths 12 with a very low risk of cross-contamination. However, by virtue of the ring of silicone 42 around the array as a whole, if a larger volume of liquid is applied to the array, as shown by the dotted outline 64, the same liquid may be allowed to enter all of the fluid inlets 25 in the array simultaneously.

One possible use of such an arrangement would be where it was desired to apply different reagents to different fluid inlets in one stage of a reaction, but to apply a common reagent or water for washing away reagents at a subsequent stage in the procedure. These two possibilities are shown respectively in Figures 8

and 9.

Figures 10, 11 and 12 show various combinations of confinement means for individual fluid inlets and arrays of inlets respectively. The embodiment of Figure 10 shows rings of hydrophobic material 40 defining confinement areas around the individual fluid inlets 12 whilst a channel 50 delimits a confinement area which contains the array of fluid inlets 12. In this embodiment, a further channel 54 may be seen inwardly of the channel 50 defining the confinement area for the array of inlets. This additional channel 54 provides a marginal increase in the fluid storage capacity above the chip.

In the embodiment of Figure 11, both the array confinement area 30 and the individual confinement areas 55 are defined by respective areas of hydrophobic material 42, 40.

By contrast, the embodiment of Figure 12 has the overall and individual confinement areas 30, 55 defined by respective channels 56, 50 around the array and individual inlets.

It will be appreciated by those skilled in the art that although several combinations of possibilities have been disclosed, the invention is not limited to these. Instead, it should be appreciated that any combination of the various possible confining means, such as geometric structure and hydrophobic material, may be employed according to the particular circumstances. In particular, it should be appreciated that whilst in the embodiment described above a particular type of confinement means is used all the way around a particular fluid inlet or array, this is not essential and, for example, it is envisaged in other embodiments that a confinement means, for example for a fluid inlet, could comprise a geometric structure on one side and hydrophobic material on another.

Claims:

1. A microfluidic device comprising a liquid inlet having an inlet mouth and liquid confinement means provided around said inlet mouth to confine liquid placed at said mouth to a predetermined area around the mouth.

2. A microfluidic device as claimed in claim 1 wherein said liquid confinement means comprises a region of hydrophobic material.

3. A microfluidic device as claimed in claim 2 wherein said region of hydrophobic material comprises a lithographically defined hydrophobic patch.

4. A microfluidic device as claimed in any preceding claim wherein said liquid confinement means comprises a geometric structure.

6. A microfluidic device as claimed in claim 5 wherein said inlet mouth is provided in a recess, the edges of said recess defining said predetermined area.

7. A microfluidic device as claimed in claim 5 or 6 wherein said liquid confinement means comprises a channel around the inlet mouth.

8. A microfluidic device comprising an array of liquid inlets as claimed in any preceding claim and a further liquid confinement means provided around said array of inlets to confine liquid placed on said array to a predetermined area around the array.

9. A microfluidic device comprising an array of liquid inlets and liquid confinement means provided around said array of inlets to confine liquid placed on said array

to a predetermined area around the array.

10. A microfluidic device as claimed in claim 8 or 9 wherein said liquid confinement means provided around said array comprises a region of hydrophobic material.

11. A microfluidic device as claimed in claim 10 wherein said region of hydrophobic material comprises a lithographically defined hydrophobic patch.

12. A microfluidic device as claimed in any of claims 8 to 11 wherein said liquid confinement means provided around said array comprises a geometric structure.

13. A microfluidic device as claimed in claim 12 wherein said array of liquid inlets is provided in a recess, the edges of said recess defining said predetermined area around the array.

14. A microfluidic device as claimed in claim 12 or 13 wherein said liquid confinement means around the array comprises a channel around the array.

15. A microfluidic device comprising a liquid inlet having an inlet mouth and a liquid confinement area around said inlet mouth such that in use liquid placed at said mouth is confined to said liquid confinement area.

16. A microfluidic device comprising a liquid inlet having an inlet mouth and a liquid confinement area around said inlet mouth, said liquid confinement area being bordered by a hydrophobic material such that in use liquid placed at said mouth is confined to said liquid confinement area by said hydrophobic material.

17. A microfluidic device comprising a liquid inlet having an inlet mouth and a liquid confinement area around said inlet mouth, said liquid confinement area being bordered by a sudden change in surface height such that in use liquid placed at said mouth is confined to said liquid confinement area by said sudden change in surface height.

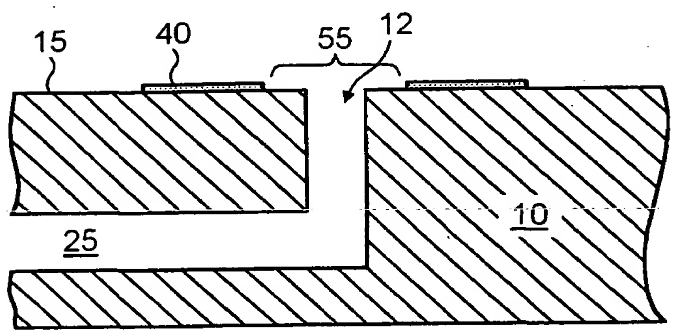

FIG. 1

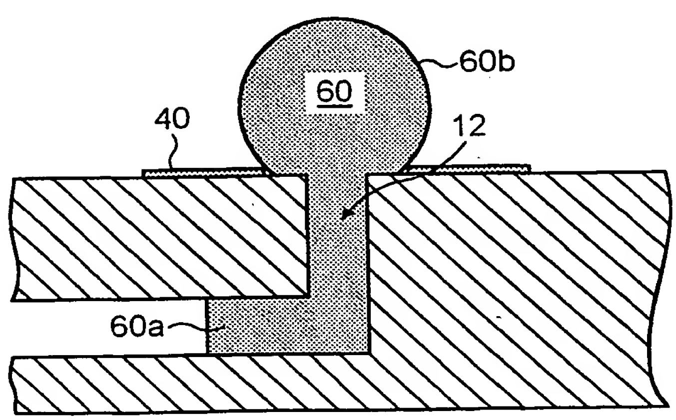

FIG. 2

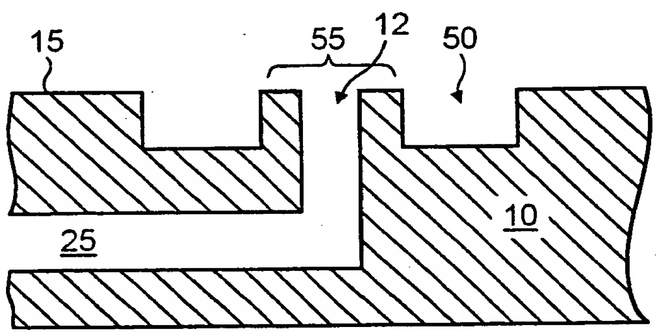

FIG. 3

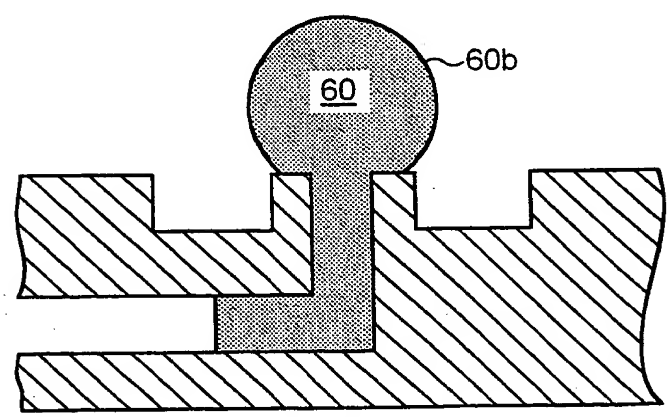

FIG. 4

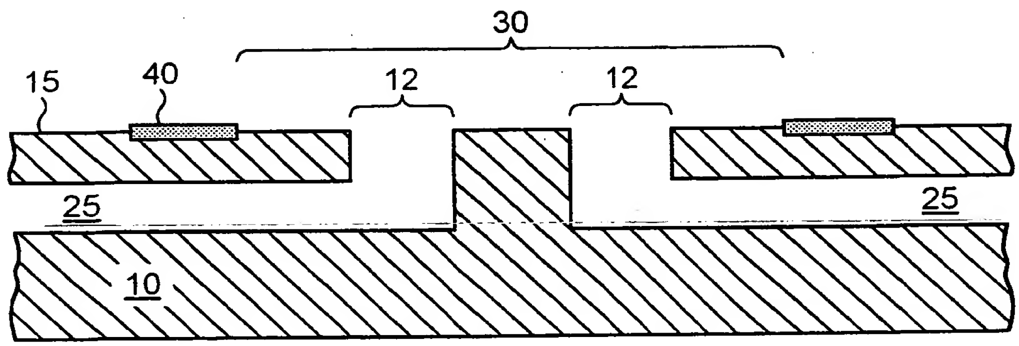

FIG. 5

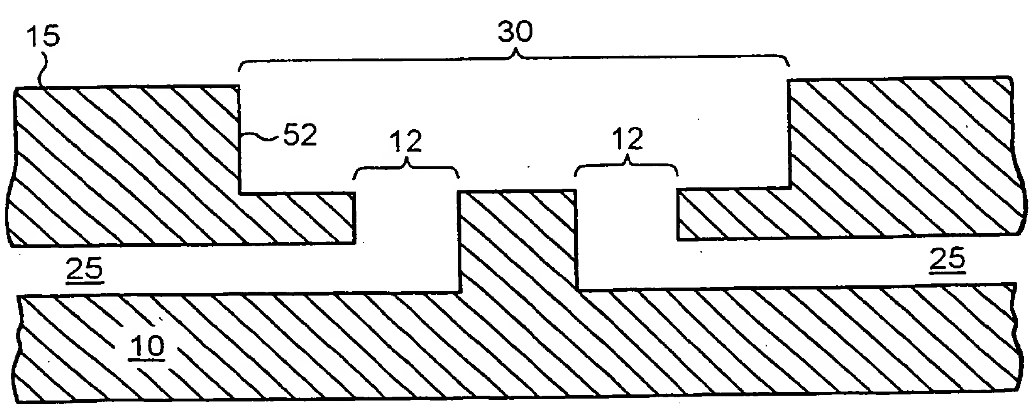

FIG. 6

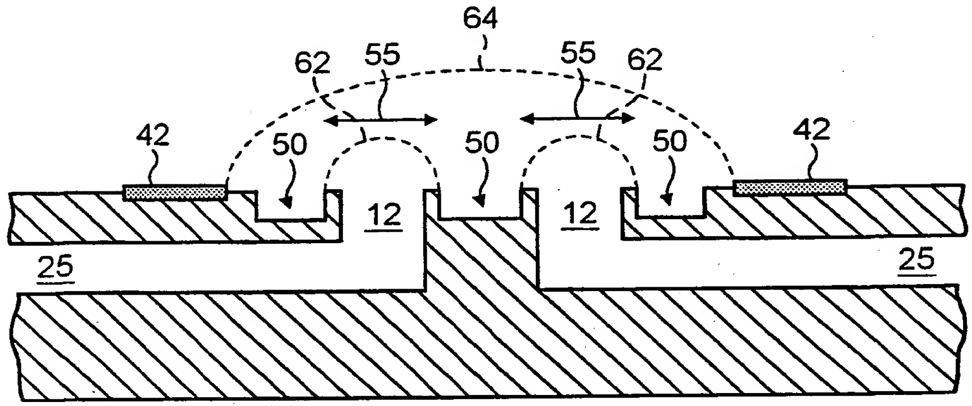

FIG. 7

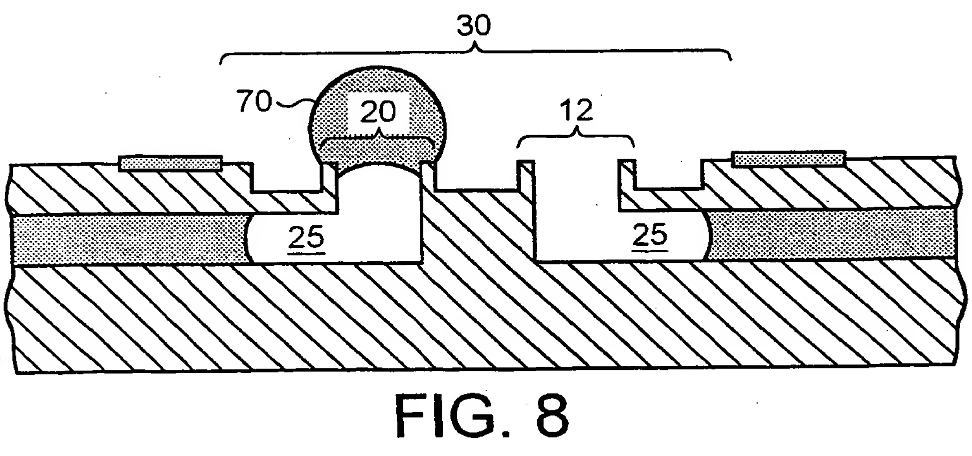

FIG. 8

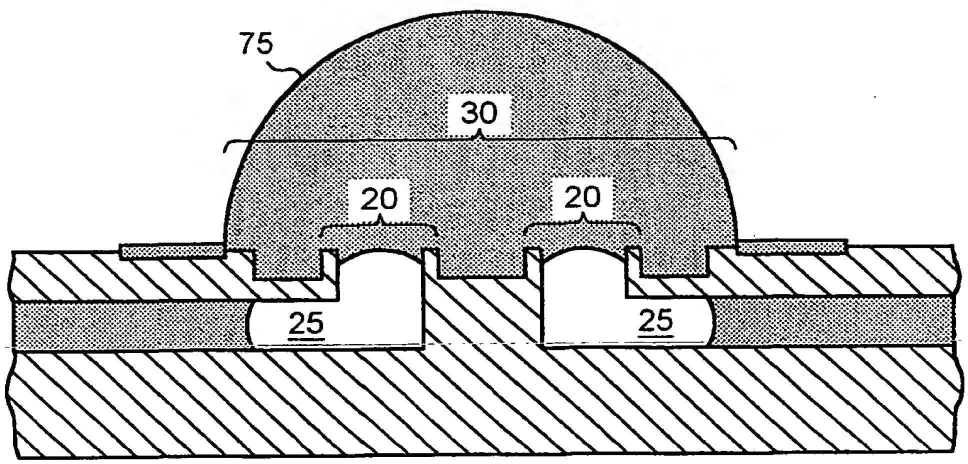

FIG. 9

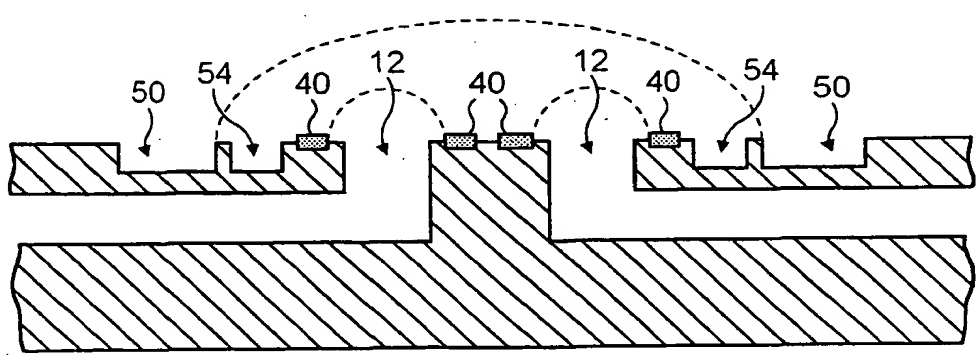

FIG. 10

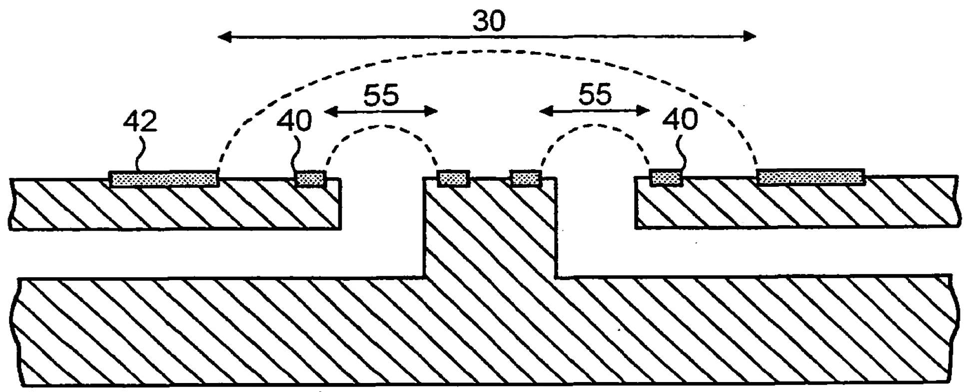

FIG. 11

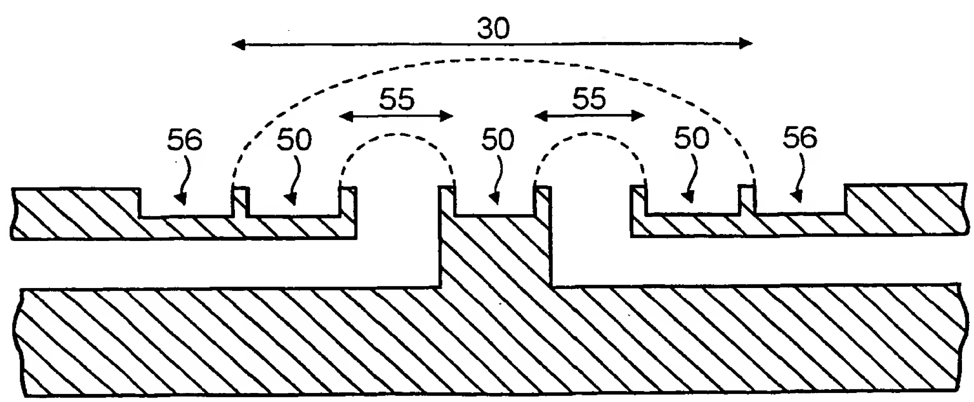

FIG. 12

INTERNATIONAL SEARCH REPORT

Int· ·onal Application No
PCT/GB 01/05222

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01L B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
14 February 2002	27/02/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Tiede, R

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